P17-09. Immunization with a Single HIV-1 Envelope Sequence Can Generate CD8+ T lymphocytes Capable of Recognizing Multiple Variant Forms of Envelope

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Poster presentation

P17-09. Immunization with a single HIV-1 envelope sequence can generate CD8+ T lymphocytes capable of recognizing multiple variant forms of envelope

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Background

The ability of CD8+ T lymphocytes to recognize a diversity of mutant forms of an HIV epitope is of central importance in the immune containment of this virus. The present studies were pursued to determine the mechanism employed by CD8+ T lymphocytes to recognize mutant viruses. In particular, we sought to determine whether mutant sequences are recognized by distinct CD8+ T lymphocyte populations or whether individual clonal populations of CD8+ T lymphocytes recognize a diversity of mutant sequences.

Methods

We employed flow cytometry, Vβ repertoire analysis, and CDR3 sequencing methodologies to characterize the clonal diversity of CD8+ T lymphocytes that recognize variant forms of the HIV-1 envelope (Env) p41A epitope generated after infection by SHIV-89.6P or elicited by HIV-1 89.6P Env immunization of Mamu-A*01+ rhesus monkeys. To evaluate the capacity of the CD8+ T lymphocytes to recognize genetically diverse isolates of HIV-1, we employed a series of tetramers constructed with variants of the p41A epitope of HIV-1 Env. To define which T cell receptor mediated the recognition of each specific variant p41A, we isolated variant p41A-specific CD8+ T lymphocyte populations and analyzed the expression of 46 Vβ families and subfamilies genes. We then determined the precise clones employed for the recognition of each variant epitope peptide through CDR3 sequencing.

Results

In both the infected and the vaccinated monkeys, we observed clonotypes capable of recognizing the majority of the variant epitope peptides.

Conclusion

These data show that exposure to a single HIV-1 Env sequence can generate clonotypes capable of recognizing multiple variant forms of HIV-1 Env. Such Env-specific CD8+ T lymphocytes should be able to confer potent, effective protection against a diverse spectrum of circulating viruses.